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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/948,393	10/10/1997	DENISA D. WAGNER	CFBF-P02-002	6939

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EXAMINER	
GAMBEL, PHILLIP	
ART UNIT	**PAPER NUMBER**
1644	

DATE MAILED: 05/03/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	08/948,393	WAGNER ET AL.	
	Examiner	Art Unit	
	Phillip Gambel	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 February 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *71,81,85,87-89,92 and 94-97* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *71,81,85,87-89,92 and 94-97* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment, filed 2/25/05, has been entered.

Claims 71, 92, 95 have been amended.

Claims 96-97 have been added.

Claims 71, 81, 85, 87-89, 92 and 94-97 are pending.

Claims 1-70, 72-80, 82-84, 86, 90, 91 and 93 have been canceled previously.

Newly submitted limitations drawn to "mimetics of PSGL-1 which resemble PSGL-1 in shape and charge distribution" are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons:

Methods of treating or inhibiting atherosclerosis with PSGL mimics (Group VII) was considered as a separate Group in the Restriction, mailed 10/10/01, and was not elected in applicant's Election, filed 1/17/02.

As pointed out previously, applicant is reminded that the instant claims have been under consideration as they read on the elected invention, drawn to methods of treating or inhibiting atherosclerosis with PSGL-1, fragments and chimeric constructs thereof and not synthetic analogs or mimetics of PSGL-1.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits.

Accordingly, that instant claims as they read on "mimetics of PSLG-1 which resemble PSGL-1 in shape and charge distribution" are withdrawn from consideration as being directed to a non-elected invention. See 37 C.F.R. § 1.142(b) and M.P.E.P. § 821.03.

Claims 71, 81, 85, 87-89, 92 and 94-97 are under consideration as they read on the elected invention, drawn to methods of treating or inhibiting atherosclerosis with PSGL-1, fragments and chimeric constructs thereof.

2. With respect to applicant's comments concerning atherosclerosis, it is understood that it has long been recognized that:

Atherosclerosis affects medium and large arteries and is characterized by patch intramural thickening of the subintima that encroaches on the arterial lumen and in its most sever form causes obstruction. The atherosclerotic plaque consists of accumulation of intracellular and extracellular lipids, smooth muscle cells, connective tissue, and glycoaminoglycans.

While two main hypothesis have been proposed to explain the pathogenesis of atherosclerosis, namely the lipid hypothesis and the chronic endothelial injury hypothesis, both of these hypotheses involved platelets and monocytes and associated growth factors.

See pages 409-413, particularly page 410, Atherosclerosis of The Merck Manual of Diagnosis and therapy, Sixteenth Edition, edited by Berkow et al., Merck Research Laboratories, Rahway, NJ 1992, pages 409-413, particularly page 410, Atherosclerosis.

Furthermore, patients with symptomatic atherosclerosis are at significant risk of stroke, myocardial infarction and peripheral artery occlusion, which primarily develop at sites of pre-existing stenosis. Atherosclerotic plaques rupture and expose tissue factor-rich plaque contents to blood. This initiates thrombus formation. Increase in fibrinogen levels correlate with thrombotic events. High levels correlate with thrombotic events. High levels may be an independent risk factor for arterial thromboembolism or a nonspecific inflammatory marker of ruptured plaques.

See page 920, column 1, Atherosclerosis of The Merck Manual of Diagnosis and Therapy, Seventeenth Edition, edited by Beers et al., Merck Research Laboratories, Whitehouse station, NJ, 1999.

De Felice et al. (Angiology 41 : 1- 11, 1990) notes that:

"It has long since been known that mural thrombi contribute to the development and progression of atherosclerotic plaque."

See page 2, Secondary Prevention of Atherosclerosis and Thrombosis.

Felice et al. also note that antiplatelet agents can influence the natural course of atherosclerosis.

See pages 2-3, Antiplatelet Agents.

As noted in the Summary of the Invention of the instant specification, the methods of instant invention include administering an agent prior to formation of an atherosclerotic lesion as well as subsequent to formation of an atherosclerotic lesion, which can include preventing growth of an atherosclerotic lesion after a surgical procedure for preventing restenosis (see page 4, paragraphs 1-2 of the instant specification).

Although applicant asserts that the claimed limitations is intended to distinguish over the prior art drawn to ischemic events rather than atherosclerosis,

applicant is reminded that the prior art clearly teaches treating atherosclerosis as well as patients undergoing surgical cardiovascular procedures with PSGL-1.

Therefore, applicant's attempts to distinguish the instant claims from the prior art by amending the claims to recite:

"A method for treating or inhibiting atherosclerosis by decreasing the formation or growth of plaque on arterial walls"

is simply amending the claims to recite a description of the same therapeutic endpoint of "treating atherosclerosis" with the same antagonistic PSGL-1 to the same patient populations, as evidenced by the Merck Manual and De Felice et al. (Angiology 41: 1- 11, 1990).

Applicant's attempts to detract from the clear teaching of treating atherosclerosis with the same PSGL-1 inhibitors as claimed is not found convincing.

Applicant's "newly amended limitations" are simply a reiteration of the instrinsic or expected characteristics of "treating or inhibiting atherosclerosis" as it reads on either the development or complications of atherosclerosis by administering PSGL-1 to the same patient populations.

It does not appear that the claim language or limitations result in a manipulative difference in the method steps when compared to the prior art disclosure. See Bristol-Myers Squibb Company v. Ben Venue Laboratories 58 USPQ2d 1508 (CAFC 2001).

3. The examiner acknowledges applicant's statement that not all inhibitors of P-selectin also function as inhibitors of E-selectin.

In addition, the examiner acknowledges the election of PSGL-1.

However, this was not a species election. The various agents were set forth in Groups, not species.

See the Restriction Requirement, mailed 10/10/01.
As pointed our previously, the following of record has been noted.
For examination purposes, the use of PSGL-1, fragments and chimeric constructs thereof have the inherent property of inhibiting E-selectin-mediated interactions.

It does not appear from the record that applicant disagrees with this assessment

4. Upon applicant's amended claims to recite "said agent being administered repeatedly in sequential doses or by the controlled release to the mammal over a period of months or years"; the previous rejection under 35 U.S.C. § 102(e) as being anticipated by Cummings et al. (U.S. Patent No. 5,464,778) has been withdrawn.

5. Claims 71, 81, 85, 87-89, 92 and 94-97 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Cummings et al. (U.S. Patent No. 5,464,778) in view of Larsen et al. (U.S. Patent No. 5,840,679), Tedder et al. (U.S. Patent No. 5,834,425), Coller et al. (U.S. Patent No. 5,976,532) and Sluiter et al. (J. Cardiovascular Pharmacology 22 (Suppl. 4): S37-S44, 1993)
essentially for the reasons set forth in the previous Office Actions and further in view of
Aberg et al. (U.S. Patent No. 5,061,694), Casscells et al. (U.S. Patent No. 5,308,622) and Hinstridge et al. (Drugs 42 (Suppl. 2): 8-2, 1991)
as it reads on applicant's newly amended claims which recite:
"said agent being administered repeatedly in sequential doses or by the controlled release to the mammal over a period of months or years"
and in further evidence of The Merck Manual of Diagnosis and Therapy, Sixteenth Edition (edited by Berkow et al., Merck Research Laboratories, Rahway, NJ 1992, pages 409-413) and De Felice et al. (Angiology 41: 1- 11, 1990)
as it reads on applicant's newly amended claims which recite:
"by decreasing the formation or growth of plaque on arterial walls".

Applicant's arguments in conjunction with the Wagner declaration under 37 C.F.R. § 1.132 (Wagner II), filed 2/25/05, have been fully considered but are not found convincing essentially for the reasons of record.

Applicant's arguments in conjunction with the previous declaration under 37 C.F.R. 1.131 (Wagner I Declaration), have been fully considered but are not found convincing essentially for the reasons of record.

Applicant's arguments and the examiner's rebuttal are essentially the same of record.

A more thorough review of applicant's arguments and the examiner's rebuttal of record can be found in the previous Office Action, mailed 10/21/04.

As indicated above,
"A method for treating or inhibiting atherosclerosis by decreasing the formation or growth of plaque on arterial walls"
is simply amending the claims to recite a description of the same therapeutic endpoint of "treating atherosclerosis" with the same antagonistic PSGL-1 for the same patient populations.

Applicant notes differences in treating restenosis which is designed to address the immediate problem of preventing a further coronary blockage resulting from the original thrombosis, while in treating atherosclerosis which is designed to prevent long term sustained arterial damage due to additional plaque buildup in the artery.
That applicant attempts to ignore the prior art teaching of treating atheroscerlosis with soluble PSGL-1 but rather focuses on the teaching of acute thrombotic complications does not take away from the clear teaching of treating atherosclerosis with PSGL by the prior art, which applicant has already acknowledged.

The prior art is consistent with the claimed invention as well as the instant disclosure as well in teaching the importance of platelet-leukocyte interactions in atherosclerosis (e.g. see columns 19-20, overlapping paragraph of Cummings et al.).
In addition, this overlapping paragraph discusses the problems of the rupture of a fully developed plaque.

Therefore, the prior art not only teaches treating atherosclerosis but also teaches addressing the problems associated with atherosclerotic plaques and the role of leukocyte-platelet interactions.

While applicant focuses on differences in the intent of treating thrombosis, restenosis and atherosclerosis, the prior art does teach treating all such complications, including patient populations under the same or nearly the same cardiovascular procedures for the same or nearly the same indications and complications with the same or nearly the same therapeutic endpoints.

Also, as indicated above with respect to atherosclerosis,
applicant's attempts to distinguish the instant claims from the prior art by amending the claims to recite:
A method for treating or inhibiting atherosclerosis "by decreasing the formation or growth of plaque on arterial walls"
is simply amending the claims to recite a description of certain underlying characteristics and elements of the same therapeutic endpoint of treating atherosclerosis.

While two main hypothesis (at least as of 1992) have been proposed to explain the pathogenesis of atherosclerosis, namely the lipid hypothesis and the chronic endothelial injury hypothesis, both of these hypotheses involved platelets and monocytes and associated growth factors.
See pages 409-413, particularly page 410, Atherosclerosis of The Merck Manual of Diagnosis and Therapy, Sixteenth Edition, edited by Berkow et al., Merck Research Laboratories, Rahway, NJ 1992, pages 409-413, particularly page 410, Atherosclerosis.

In addition, De Felice et al. (Angiology 41: 1- 11, 1990) notes that:
"It has long since been known that mural thrombi contribute to the development and progression of atherosclerotic plaque."
See page 2, Secondary Prevention of Atherosclerosis and Thrombosis.
Felice et al. also note that antiplatelet agents can influence the natural course of atherosclerosis.
See pages 2-3, Antiplatelet Agents.

As noted in the Summary of the Invention of the instant specification, the methods of instant invention include administering an agent prior to formation of an atherosclerotic lesion as well as subsequent to formation of an atherosclerotic lesion, which can include preventing growth of an atherosclerotic lesion after a surgical procedure for preventing restenosis (see page 4, paragraphs 1-2 of the instant specification).

Although applicant asserts that the claimed limitations is intended to distinguish over the prior art drawn to ischemic events rather than atherosclerosis, applicant is reminded that the prior art clearly teaches treating atherosclerosis as well as patients undergoing surgical cardiovascular procedures with PSGL-1.

Therefore, applicant's attempts to distinguish the instant claims from the prior art by amending the claims to recite:
"A method for treating or inhibiting atherosclerosis by decreasing the formation or growth of plaque on arterial walls"
is simply amending the claims to recite an intrinsic description of the same therapeutic endpoint of "treating atherosclerosis" with the same antagonistic PSGL-1 to the same patient populations.

Applicant's attempts to detract from the clear teaching of treating atherosclerosis with the same PSGL-1 inhibitors as claimed is not found convincing.

Applicant's "newly amended limitations" are simply a reiteration of the intrinsic or expected characteristics of "treating or inhibiting atherosclerosis" as it reads on either the development or complications of atherosclerosis by administering PSGL-1 to the same patient populations.

The following is noted with respect to the newly amended limitation of:
"said agent being administered repeatedly in sequential doses or by the controlled release to the mammal over a period of months or years".

With respect to Cummings et al. of record,
Further, it is noted that Cummings et al. teach various formulations of inhibitors including those for slow release over a period of time, including months (see columns 20-21, overlapping paragraph).
Also, that treatment is dictated by the specific condition and will generally follow standard medical practices (e.g. see column 21, paragraph 1).

As pointed out previously, Coller et al. teach the art known vessel-corrective techniques at the time the invention was made in the treatment of cardiovascular disorders such as atherosclerosis and reocclusion, including angioplasty, atherectomy and coronary bypass surgery (see Background of the Invention on column 1 and Utility of Platelet-specific Chimeric Immunoglobulin on columns 5-7).
In teaching the use of an inhibitor of platelet aggregation and thrombus formation associated with such conditions, Coller et al. teach the art known use of combination therapy with other drugs such as thrombolytic agents and that the amounts administered before, along with or subsequent to treatment will depend on a variety of factors and clinical symptoms known to the ordinary artisan at the time the invention was made (see column 6, paragraphs 2-3).

In contrast to applicant's assertions, Cummings et al. and Coller et al. are drawn to the same or similar methods of inhibiting platelet-leukocyte / endothelial interactions for various clinical applications, including atherosclerosis and ischemia, myocardial infarction and reperfusion injury as well as cardiovascular disorders such as atherosclerosis, including angioplasty, atherectomy and coronary bypass surgery.

Again, it does not appear that the claim language or limitations result in a manipulative difference in the method steps when compared to the prior art disclosure. See Bristol-Myers Squibb Company v. Ben Venue Laboratories 58 USPQ2d 1508 (CAFC 2001).

The following prior art provide the well known practice of providing treatment to meet the needs of the patient by the ordinary artisan and in the context of the treatment of atherosclerosis, this included prolonged treatment over a period of months or years.

"A method for treating or inhibiting atherosclerosis by decreasing the formation or growth of plaque on arterial walls"
is simply amending the claims to recite a description of the same therapeutic endpoint of "treating atherosclerosis" with the same antagonistic PSGL-1.

Aberg et al. (U.S. Patent No. 5,061,694), Casscells et al. (U.S. Patent No. 5,308.622) and Hinstridge et al. (Drugs 42 (Suppl. 2): 8-2, 1991) have been added to address applicant's newly amended claim limitation:
"said agent being administered repeatedly in sequential doses or by the controlled release to the mammal over a period of months or years.

Gunnar et al. teach in the slowing the progress of atherosclerosis, including the reduction or eliminating atherosclerotic lesions (see entire document, particularly Summary of the Invention) that :

The formulations will be administered for prolonged periods, that is, for as long as it is necessary to treat the atherosclerosis. Sustained release forms of such formulations which may provide such amounts biweekly, weekly, monthly and the like may also be employed. A dosing period of at least one to two weeks are required to achieve minimal benefit.

See column 5, lines 55-61.

Casscells et al. teach in the inhibition of platetet adherence and aggregations in a number of disease states, including atherosclerosis (see entire document, including Summary of the Invention) that:

The exact effective dosage varies with the patient's weight and may be influenced by a number of factors, including the route of administration, type and state of disease and overall health status of the particular patient:

See column 15, lines 10-16.

Hinstridge et al. provide An Overview of Therapeutic Interventions in Myocardial Infarction, Empahsis on Secondary Prevention, including treatment regimens for the prevention of further occlusion, infarction and death by preventing subsequent thrombosis and atherosclerosis (see page 9, column 1, paragraph 2) including the use of Antiplatelet Drugs that can be administered for 1-2 years (see pages 14-15, including page 14, column 2, paragraph 3).

In addition to the long-term treatment with anti-platelet agents in the treatment of cardiovascular patients, including those with atherosclerosis, addressed above;

given the long term chronic nature of atherosclerosis, it would have been obvious to one of ordinary skill in the art at the time the invention was made to provide prolonged treatment of an appropriate inhibitor to meet the needs of the patient and the particular state of disease, which has been standard practice by the medical profession.

Given the art known practice of modes of administration and dosing depending on a variety of factors and clinical symptoms known to the ordinary artisan at the time the invention was made, as taught by Coller et al. In cardiovascular diseases, the claimed limitations were met or would have been obvious variants in meeting the needs of the patients in order to achieve a therapeutic effect depending on the symptom at the time the invention was made.

From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

With respect to applicant's arguments concerning the secondary references, once a prima facie case of obviousness has been made the burden of going further is shifted to applicant. In re Keller, 208 USPQ 871, 882 (CCPA 1981). This applicant has not done, but rather argues the references individually and not their combination. One cannot show non-obviousness by attacking references individually where the rejections are based on a combination of references. In re Young, 150 USPQ 725 (CCPA 1968). See MPEP 2145.

Applicant's arguments have not been found persuasive for the reasons of record.

6. Claims 71, 81, 85, 87-89, 92 and 94-97 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over
claims 40-41, 49-52, 59-60 and 73 (or appropriate pending claims) as they read on the use of PSGL-1 to treat atherosclerosis of copending application Serial No. 09/436 for the reasons of record.

Although the conflicting claims are not identical, they are not patentably distinct from each other because they are drawn to the same or nearly the same methods of treating atherosclerosis with the same or nearly the same PSGL-1, fragments and chimeric constructs thereof.

This is a *provisional* obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

The previous provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over1 to treat atherosclerosis of copending application USSN 09/883,642 has been withdrawn in view of limiting the methods of treating atherosclerosis to the use of antagonistic PSGL-1 in the instant application and to the use of antagonistic anti-PSGL-1 antibodies in copending USSN 09/883,642.

Applicant's amendment, filed 2/25/05, indicates that it is premature to formulate a detailed response. However, applicant affirms their intent to file a terminal disclaimer in this application to overcome this rejection provided that the apaplication is otherwise considered to be in proper condition for allowance.

7. No claim is allowed

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).
A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (571) 272-0844. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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April 28, 2005